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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,005	12/30/2003	Herbert T. Nagasawa	30451.2USU1	9934

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EXAMINER	
HEARD, THOMAS SWEENEY	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/750,005	**Applicant(s)** NAGASAWA ET AL.	
	Examiner Thomas S. Heard	**Art Unit** 1654	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 July 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See cont'n sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-4,9,10,20,21,25,26,46,50 and 51*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:

    _____
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

8/2/07
ANISH GUPTA
PRIMARY EXAMINER

Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the 103(a) rejection for reasons of record and the argumets presented herein. Applicants have argued on page 10 of their remarks in February 15, 2007 and again in this After Final amendment on page 11 that the prior art references do not suggest the instantly claimed invention and that the reasoning falsely assumes the following:
(1) there is similarity between CSSG and CySSME which would suggest their interehangeability;
(2) there is motivation to use sulfhydryl protected glutathione prodrug instead of a prodrug; and
(3) motivation exists to use sulflaydryl protected glutathione prodrug .to reduce oxidative stress.
In addressing (1), there is similarity as both release cysteine, a precursos to GSH and an essential component for maintaining GSH levels and reducing oxidative stress. In addressing (2) and (3), motivation was specifically addressed and is repeated here:
"Given that CySSG releases Cysteine, it appears that CySSG could be considered a sulfhydryl protected cysteine prodrug as well as a sulfhydryl protected glutathione prodrug. That fact that the Applicants are arguing a mechanism of how CySSG (CSSG) raised GSH levels, it does not make it patentable because when Jonas et al added CySSG (CSSG) to the cell, it would have been producing GSH along with Cysteine, and the Cysteine it produced would also make GSH. Applicants are arguing a latent property of CySSG (CSSG) to release GSH in addition to Cysteine. CySSG (CSSG) and CySSME both share the common property to release/produce cysteine in the cell, leading to GSH levels which are important for oxidative stress management and provides the motivation to use either one. Again, the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). See also In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) (setting forth test for implicit teachings); In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) (discussion of reliance on legal precedent); In re Nilssen, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (references do not have to explicitly suggest combining teachings); Ex parte Clapp, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985) (examiner must present convincing line of reasoning supporting rejection); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (reliance on logic and sound scientific reasoning). The use of CySSG (CSSG) in place of CySSME does flow logically as both increase Cysteine, and the increase in cysteine leads to increased GSH.

Applicant's arguments regarding "Benefits of Using a Sulfhydryl Protected Glutathione Prodrug" in stating that "prior to the present invention, it was not obvious that sulfhydryl protected glutathione prodrugs were a readily available and efficient source of GSH to a cell nor to administer a sulfhydryl protected glutathione prodrug such as CSSG since, among other things, it had not been known whether the enzymatic reduction (or enzyme-catalyzed thiol- disulfide interchange reaction) velocity of CSSG would be sufficiently fast and efficient to replenish GSH." CSSG is a natural product found in the cell, is readily available, and not a prodrug. Further, the compound had been administered prior to the Applicants invention was shown to produce cysteine, essential for GSH production.

Applicant's arguments regarding "There Was No Reasonable Expectation of Success for the Substitution of a Sulfhydryl Protected Glutathione Prodrug for a Cysteine Prodrug" on page 13 of Applicant's response has been addressed in the previous office action and briefly restated here: "Both CySSME and CYSSG (CSSH) were shown by the prior references to produce an increase in cysteine levels which are important for producing GSH. Therefore, it worked and was successful. Applicants arguments that derive from (Crankshaw et al., J Biochem Mol Tox, 2002, 16(5):235-244 (Exhibit 1 submitted with Applicant's July 11, 2007 response which has already been considered in the IDS and is therefore not entered) that state the not all compounds can produce or increase cysteine levels is not persuasive because the references used in the 103(a) rejection show that they do increase cysteine levels and are not the same compounds as those of CySSME and CYSSG.

Therefore, the 103(a) rejection set forth in the Office Action mailed 4/11/2007 is maintained.